AMENDMENT TO THE CLAIMS

1. (**Currently Amended**) An adzyme for inhibiting an activity of a substrate polypeptide, the adzyme being an immunoglobulin fusion complex comprising: a first fusion protein bound to a second fusion protein, wherein the first fusion protein comprises a constant portion of an immunoglobulin heavy chain and a protease domain that catalyzes the proteolytic cleavage of at least one peptide bond of the substrate polypeptide so as to inhibit the activity of the polypeptide, and wherein the second fusion protein comprises a constant portion of an immunoglobulin heavy chain and a targeting domain that reversibly binds with ~~an address~~ a site on said substrate polypeptide, wherein said targeting domain and said protease domain are discrete and heterologous with respect to each other, and wherein ~~said adzyme is resistant to cleavage by said protease domain~~ said adzyme comprises at least one amino acid substitution or posttranslation modification to inhibit auto-cleavage by said protease domain.

2. (**Canceled**)

3. (**Withdrawn**) The adzyme of claim 1, wherein said protease domain is a zymogen.

4. (**Original**) The adzyme of claim 1, wherein said protease domain is selected from among: a serine proteinase and a metalloproteinase.

5. (**Original**) The adzyme of claim 1, wherein said adzyme is purified from a cell culture in the presence of a reversible protease inhibitor that inhibits the protease activity of the protease domain.

6-18. (**Canceled**)

19. (**Previously Presented**) The adzyme of claim 1, wherein the substrate polypeptide is an extracellular polypeptide, and wherein said activity is receptor-mediated signaling activity.

20. (**Canceled**)

21. (**Previously Presented**) The adzyme of claim 1, wherein said substrate polypeptide is present in biological fluid of an animal.

22. (**Original**) The adzyme of claim 21, wherein said biological fluid is blood or lymph.

23. (**Previously Presented**) The adzyme of claim 21, wherein said substrate polypeptide is a polypeptide hormone, a growth factor and/or a cytokine.

24. (**Previously Presented**) The adzyme of claim 21, wherein said substrate polypeptide is selected from among: four-helix bundle factors, EGF-like factors, insulin-like factors, β-trefoil factors and cysteine knot factors.

25. (**Previously Presented**) The adzyme of claim 21, wherein said substrate polypeptide is an inflammatory cytokine and said adzyme reduces the pro-inflammatory activity of said substrate.

26. (**Previously Presented**) The adzyme of claim 1, wherein the targeting domain is an antibody or polypeptide(s) including an antigen binding site of an antibody.

27. (**Previously Presented**) The adzyme of claim 1, wherein the targeting moiety is selected from the group consisting of a monoclonal antibody, an Fab, an $F(ab)_2$, an scFv, a heavy chain variable region and a light chain variable region.

28. (**Withdrawn**) The adzyme of claim 1, wherein said substrate polypeptide is a receptor ligand, and said targeting domain includes a ligand binding domain of a cognate receptor of said ligand.

29. (**Withdrawn**) The adzyme of claim 1, wherein said targeting domain is an artificial protein or peptide sequence engineered to bind to said substrate.

30. (**Previously Presented**) The adzyme of claim 1, wherein the substrate polypeptide is endogenous to a human patient.

31. (**Previously Presented**) The adzyme of claim 30, wherein the effect of the adzyme on the substrate polypeptide is not significantly affected by the presence of a human serum protein when tested with a concentration of the substrate polypeptide that is about 0.5 to 2

times the expected physiological concentration of the substrate polypeptide and a concentration of the human serum protein that is about 0.5 to 2 times the expected physiological concentration of the human serum protein.

32. (**Previously Presented**) The adzyme of claim 31, wherein the human serum protein is human serum albumin.

33. (**Previously Presented**) The adzyme of claim 1, wherein said adzyme alters the half-life of the substrate polypeptide *in vivo*.

34. (**Previously Presented**) The adzyme of claim 1, which alters an interaction between the substrate polypeptide and a receptor.

35-36. (**Canceled**)

37. (**Original**) A pharmaceutical preparation comprising the adzyme of claim 1 and a pharmaceutically effective carrier.

38. (**Original**) The pharmaceutical preparation of claim 37, formulated such that autocatalytic proteolysis of the adzyme is inhibited.

39. (**Original**) The pharmaceutical preparation of claim 38, further comprising a reversible inhibitor of said protease domain.

40. (**Original**) The pharmaceutical preparation of claim 39, wherein the reversible inhibitor is safe for administration to a human patient.

41. (**Canceled**)

42. (**New**) The adzyme of claim 1, wherein said amino acid substitution or posttranslation modification is in said targeting domain, said protease domain, said immunoglobulin heavy chain, or a linker.

43. (**New**) The adzyme of claim 1, wherein said substrate polypeptide is part of an insoluble protein containing complex.